

DOCKET NO.: CEPH-3134
Application No.: 10/698,625
Office Action Dated: May 24, 2006

PATENT

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REMARKS**AUG 23 2006**

Following entry of the foregoing amendments, claims 24, 26 to 35, and 43 to 45 will be pending in the application. Claims 24, 26 to 32, 35, and 43 to 45 have been amended, and claims 25, 36 to 42, and 46 have been canceled, herein. No new claims have been added. Support for the amendments is found throughout the specification as originally filed. The first paragraph of the specification has been amended to update the priority information. No new matter has been added.

Applicants respectfully request reconsideration of the rejections of record in view of the foregoing amendments and the following remarks.

Alleged Anticipation

Claim 24 has been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Stephens, et al., *Ann. Intern. Assoc.* 9, 1936, 1488-1502 ("the Stephens article"). Without conceding the correctness of the rejection, and to advance prosecution, claim 24 has been amended to recite methods of treating acute myelogenous leukemia in humans that comprise administering a combination of a therapeutically effective amount of arsenic trioxide and radiation. The Stephens article describes treatment of chronic myelogenous leukemia with potassium arsenite (Fowler's solution), supplemented with radiation treatment. Since the Stephens article fails to teach or suggest methods of treating acute myelogenous leukemia with a combination of arsenic trioxide and radiation, Applicants respectfully request withdrawal of the rejection.

Alleged Obviousness

A. Claims 24 to 39 and 42 to 45 have been rejected under 35 U.S.C. § 103(a) as allegedly obvious over Zhang, U.S. Patent number 6,720,011 ("the Zhang patent"); Kwong, Y.L., et al., *Blood* 89, 1997, 3487-3488 ("the Kwong article"); and Chen, G., et al., *Blood* 89, 1997, 3345-3353 ("the Chen article") in view of the Stephens article and Medline abstract number 83131994 ("the Medline abstract").

As discussed above, claim 24 has been amended to recite methods of treating acute myelogenous leukemia in humans that comprise administering a combination of a therapeutically effective amount of arsenic trioxide and radiation. Applicants respectfully request

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reconsideration and withdrawal of the rejection because those skilled in the art would not have been motivated to combine the teachings of the cited references when attempting to develop treatments for acute myelogenous leukemia. For example, the Zhang patent and the Chen article describe treatment of acute promyelocytic leukemia (APL), a type of acute myelogenous leukemia, with arsenic trioxide, but do not suggest combining radiation therapy with arsenic trioxide for the treatment of APL. The Kwong article reports that arsenic trioxide has been used to treat APL and chronic myeloid leukemia, but does not suggest combining radiation therapy with arsenic trioxide for treatment of APL or chronic myeloid leukemia. The Stephens article describes treatment of *chronic* myelogenous leukemia with potassium arsenite (Fowler's solution), supplemented with radiation, but does not describe treatment of AML, much less suggest treatment of AML with a combination of arsenic trioxide and radiation.

The Medline abstract describes experiments in which the effect of radiation on two acute myelogenous leukemia (AML) cell lines and on a normal stem cell line was compared. The abstract reports that little difference existed in the radiosensitivity of the stem and acute myelogenous leukemia cell lines, but states that the effect of radiation on the growth of the acute myelogenous leukemia cells was *stimulatory*. The authors concluded that "residual AML cells surviving chemotherapy...will rapidly repopulate the irradiated host." The Medline abstract thus indicates that *radiotherapy stimulated the growth of acute myelogenous leukemia cells* and suggests that use of radiotherapy for the treatment of acute myelogenous leukemia following chemotherapy would likely be detrimental since the growth of any AML cells that survived chemotherapy would likely be stimulated by subsequent radiation therapy. The Medline abstract thus teaches away from treating acute myelogenous leukemia with a combination of chemotherapy (with agents such as arsenic trioxide) and radiation. Those skilled in the art, upon review of the abstract's teachings, would therefore not have been motivated to combine the teachings of the Zhang patent and the Kwong, Chen, and Stephens articles, and accordingly, would not have been motivated to treat AML with a combination of arsenic trioxide and radiation. Applicants accordingly, respectfully request withdrawal of the rejection.

B. Claims 24 to 39 and 42 to 45 have been rejected under 35 U.S.C. § 103(a) as allegedly obvious over the Zhang patent and the Kwong and Chen articles in view of the Stephens article and Witte, et al., U.S. patent number 4,599,305 ("the Witte patent"). Applicants respectfully request reconsideration and withdrawal of the rejection because a combination of the

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cited references fails to teach or suggest every limitation of the amended claims. For example, as discussed above, the Zhang patent and the Kwong and Chen articles fail to suggest combining radiation treatment with arsenic trioxide for treatment of APL. The Stephens article does not describe treatment of AML, much less suggest treatment of AML with a combination of arsenic trioxide and radiation. The Witte patent states that "acute leukemia requires immediate treatment utilizing the full range of therapeutic measures available,"¹ but fails to teach or suggest that "the full range of therapeutic measures" would involve a *combination of* arsenic trioxide and radiation. When considered alone or in combination, the cited references thus fail to teach or suggest every limitation of the amended claims, and Applicants accordingly, respectfully request withdrawal of the rejection.

Conclusion

Applicants believe that the foregoing constitutes a complete and full response to the Office action of record. An early and favorable action is therefore respectfully requested.

Respectfully submitted,



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